

Attorney's Docket No: **B1055/7004 (JRV)**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Lipscombe et al.  
Serial No: Not assigned  
Filed: Herewith  
For: HUMAN N-TYPE CALCIUM CHANNEL ISOFORM AND USES THEREOF  
Examiner: Unknown  
Art Unit: Unknown

Box PATENT APPLICATION  
Commissioner for Patents  
Washington, D.C. 20231

**PRELIMINARY AMENDMENT**

Please amend the application as follows.

**In the Claims**

Please delete without prejudice claims 1-4, 16, 17, 20, 22-28, 30 and 35.

Please amend the claims as follows. Applicants have included herewith pages showing markups of the claims with insertions and deletions indicated by underlining and bracketing, respectively.

5.(amended) An isolated human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid molecule which encodes a human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit polypeptide which comprises SEQ ID NO:2 in an extracellular domain.

6.(amended) The isolated human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid molecule of claim 5, wherein the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:1.

7.(amended) The isolated human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid molecule of claim 5, wherein the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:3.

8.(amended) The isolated human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid molecule of claim 5, wherein the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid molecule consists of the nucleotide sequence of SEQ ID NO:3.

9.(amended) The isolated human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid molecule of claim 8, wherein the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid is a homolog or allele of the nucleic acid sequence of SEQ ID NO:3.

10.(amended) An isolated fragment of the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid molecule of claim 5.

11.(amended) An expression vector comprising the isolated human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid molecule of claim 5 operably linked to a promoter.

12.(amended) An expression vector comprising the isolated human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid molecule of claim 10 operably linked to a promoter.

14.(amended) An agent which selectively binds a human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit polypeptide which comprises SEQ ID NO:2 in an extracellular domain or the nucleic acid of claim 5.

18.(amended) The agent of claim 14, wherein the agent is an antisense nucleic acid which selectively binds to the nucleic acid of claim 5.

19.(amended) The agent of claim 14, wherein the agent is an inhibitor of the calcium channel activity of the human N-type calcium channel  $h\alpha_{1B+SFVG}$  subunit polypeptide.

31.(amended) A method for identifying compounds which selectively bind a human N-type calcium channel  $h\alpha_{1B+SFVG}$  subunit isoform comprising,

providing a first cell or membrane encapsulated space which expresses a human N-type calcium channel  $h\alpha_{1B+SFVG}$  subunit isoform encoded by the nucleic acid molecule of claim 5,

providing a second cell or membrane encapsulated space which expresses a human N-type calcium channel non- $h\alpha_{1B+SFVG}$  subunit isoform, wherein the second cell or membrane encapsulated space is identical to the first cell except for the  $\alpha_{1B}$  isoform expressed,

contacting the first cell or membrane encapsulated space and the second cell or membrane encapsulated space with a compound,

determining the binding of the compound to the first cell or membrane encapsulated space and the second cell or membrane encapsulated space, wherein a compound which binds the first cell or membrane encapsulated space but does not bind the second cell or membrane encapsulated space is a compound which selectively binds the human N-type calcium channel  $h\alpha_{1B+SFVG}$  subunit isoform.

32.(amended) A method for identifying compounds which selectively bind a human N-type calcium channel  $h\alpha_{1B+SFVG}$  subunit isoform comprising,

providing a human N-type calcium channel  $h\alpha_{1B+SFVG}$  subunit isoform polypeptide encoded by the nucleic acid molecule of claim 5 or the nucleic acid molecule of claim 5,

providing a human N-type calcium channel non- $h\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid,

contacting the human N-type calcium channel  $h\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid and the human N-type calcium channel non- $h\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid with a compound,

determining the binding of the compound to the human N-type calcium channel  $h\alpha_{1B+SFVG}$

subunit isoform polypeptide or nucleic acid and the human N-type calcium channel non- $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid, wherein a compound which binds the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid but does not bind the human N-type calcium channel non- $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid is a compound which selectively binds the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform.

33.(amended) A method for identifying compounds which preferentially bind a human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform comprising,

providing a first cell or membrane encapsulated space which expresses a human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform encoded by the nucleic acid molecule of claim 5,

providing a second cell or membrane encapsulated space which expresses a human N-type calcium channel non- $\alpha_{1B+SFVG}$  subunit isoform, wherein the second cell or membrane encapsulated space is identical to the first cell except for the  $\alpha_{1B}$  isoform expressed,

contacting the first cell or membrane encapsulated space and the second cell or membrane encapsulated space with a compound,

determining the binding of the compound to the first cell or membrane encapsulated space and the second cell or membrane encapsulated space, wherein a compound which binds the first cell or membrane encapsulated space in an amount greater than the compound binds the second cell or membrane encapsulated space is a compound which preferentially binds the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform.

34.(amended) A method for identifying compounds which preferentially bind a human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform comprising,

providing a human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform polypeptide encoded by the nucleic acid molecule of claim 5 or the nucleic acid molecule of claim 5,

providing a human N-type calcium channel non- $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid,


contacting the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid and the human N-type calcium channel non- $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid with a compound,

determining the binding of the compound to the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid and the human N-type calcium channel non- $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid, wherein a compound which binds the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid in an amount greater than the human N-type calcium channel non- $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid is a compound which preferentially binds the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform.

**Remarks**

Please enter this amendment prior to calculation of the fees. The claims were amended to reduce claims fees. No new matter has been added.

Respectfully submitted,

  
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### Amended Claims

5.(amended) An isolated human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid molecule which encodes [the polypeptide of any of claims 1-4] a human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit polypeptide which comprises SEQ ID NO:2 in an extracellular domain.

6.(amended) The isolated human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid molecule of claim 5, wherein the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:1.

7.(amended) The isolated human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid molecule of claim 5, wherein the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:3.

8.(amended) The isolated human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid molecule of claim 5, wherein the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid molecule consists of the nucleotide sequence of SEQ ID NO:3.

9.(amended) The isolated human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid molecule of claim 8, wherein the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid is a homolog or allele of the nucleic acid sequence of SEQ ID NO:3.

10.(amended) An isolated fragment of the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid molecule of claim 5.

11.(amended) An expression vector comprising the isolated human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit nucleic acid molecule of claim 5 operably linked to a promoter.

12.(amended) An expression vector comprising the isolated human N-type calcium channel

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$\alpha_{1B+SFVG}$  subunit nucleic acid molecule of claim 10 operably linked to a promoter.

14.(amended) An agent which selectively binds [the] a human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit polypeptide [of claim 1] which comprises SEQ ID NO:2 in an extracellular domain or [a] the nucleic acid [that encodes the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit polypeptide] of claim [1] 5.

18.(amended) The agent of claim 14, wherein the agent is an antisense nucleic acid which selectively binds to [a] the nucleic acid of claim 5 [encoding the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit polypeptide].

19.(amended) The agent of claim[s] 14[-18], wherein the agent is an inhibitor of the calcium channel activity of the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit polypeptide.

31.(amended) A method for identifying compounds which selectively bind a human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform comprising,

providing a first cell or membrane encapsulated space which expresses a human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform encoded by the nucleic acid molecule of claim 5,

providing a second cell or membrane encapsulated space which expresses a human N-type calcium channel non- $\alpha_{1B+SFVG}$  subunit isoform, wherein the second cell or membrane encapsulated space is identical to the first cell except for the  $\alpha_{1B}$  isoform expressed,

contacting the first cell or membrane encapsulated space and the second cell or membrane encapsulated space with a compound,

determining the binding of the compound to the first cell or membrane encapsulated space and the second cell or membrane encapsulated space, wherein a compound which binds the first cell or membrane encapsulated space but does not bind the second cell or membrane encapsulated space is a compound which selectively binds the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform.

32.(amended) A method for identifying compounds which selectively bind a human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform comprising,

providing a human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform polypeptide encoded by the nucleic acid molecule of claim 5 or the nucleic acid molecule of claim 5,

providing a human N-type calcium channel non- $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid,

contacting the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid and the human N-type calcium channel non- $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid with a compound,

determining the binding of the compound to the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid and the human N-type calcium channel non- $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid, wherein a compound which binds the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid but does not bind the human N-type calcium channel non- $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid is a compound which selectively binds the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform.

33.(amended) A method for identifying compounds which preferentially bind a human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform comprising,

providing a first cell or membrane encapsulated space which expresses a human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform encoded by the nucleic acid molecule of claim 5,

providing a second cell or membrane encapsulated space which expresses a human N-type calcium channel non- $\alpha_{1B+SFVG}$  subunit isoform, wherein the second cell or membrane encapsulated space is identical to the first cell except for the  $\alpha_{1B}$  isoform expressed,

contacting the first cell or membrane encapsulated space and the second cell or membrane encapsulated space with a compound,

determining the binding of the compound to the first cell or membrane encapsulated



space and the second cell or membrane encapsulated space, wherein a compound which binds the first cell or membrane encapsulated space in an amount greater than the compound binds the second cell or membrane encapsulated space is a compound which preferentially binds the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform.

34.(amended) A method for identifying compounds which preferentially bind a human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform comprising,

providing a human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform polypeptide encoded by the nucleic acid molecule of claim 5 or the nucleic acid molecule of claim 5,

providing a human N-type calcium channel non- $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid,

contacting the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid and the human N-type calcium channel non- $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid with a compound,

determining the binding of the compound to the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid and the human N-type calcium channel non- $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid, wherein a compound which binds the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid in an amount greater than the human N-type calcium channel non- $\alpha_{1B+SFVG}$  subunit isoform polypeptide or nucleic acid is a compound which preferentially binds the human N-type calcium channel  $\alpha_{1B+SFVG}$  subunit isoform.